# Efficacy and Safety of Intravesical Cretostimogene Grenadenorepvec Plus Gemcitabine in High-Risk BCG-Exposed Or BCG-Unresponsive Non-Muscle Invasive Bladder Cancer

## CORE-008 Cohort CX

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Presented at the New England Section of the American Urological Association Annual Meeting

October 24, 2026

Dana-Farber Cancer Institute | Mass General Brigham

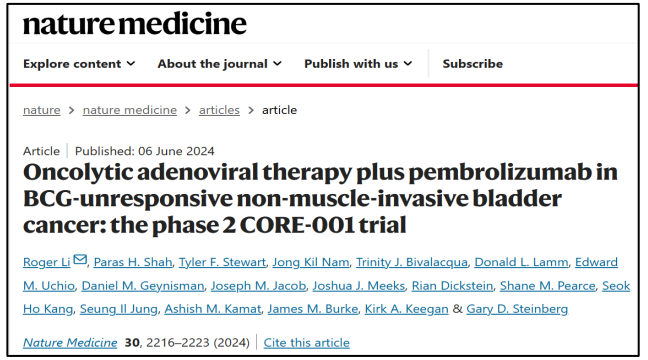
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# Disclosures

- CG Oncology: Clinical trial investigator, consultant
- Urogen: Advisory board
- Watershed: Steering committee, stocks
- Ferring: Advisory board, research support
- Pfizer: Advisory board
- MGB MIT: Research funding

# Rationale for Novel Intravesical Combination Strategies in HR-NMIBC

- Published evidence supports efficacy and safety of cretostimogene monotherapy and in combination with pembrolizumab for HR BCG-UR NMIBC and nivolumab for MIBC.[1-3]
- Novel intravesical therapeutic approaches that leverage complementary mechanisms and immune-modulating synergy are still needed for HR NMIBC.
- Pre-clinical data supports mechanistic rationale for combining intravesical gemcitabine and cretostimogene.


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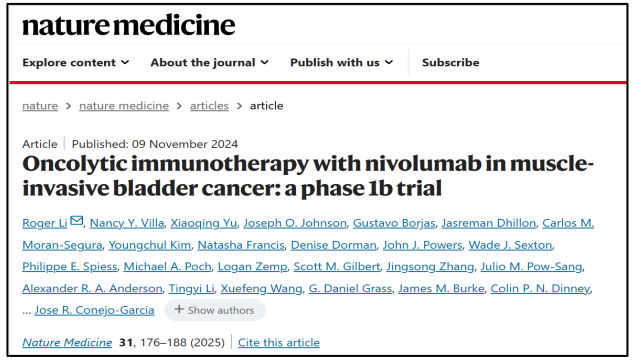
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Article | Published: 06 June 2024

**Oncolytic adenoviral therapy plus pembrolizumab in BCG-unresponsive non-muscle-invasive bladder cancer: the phase 2 CORE-001 trial**

Roger Li, Paras H. Shah, Tyler F. Stewart, Jong Kil Nam, Trinity J. Bivalacqua, Donald L. Lamm, Edward M. Uchio, Daniel M. Geynisman, Joseph M. Jacob, Joshua J. Meeks, Rian Dickstein, Shane M. Pearce, Seok Ho Kang, Seung Il Jung, Ashish M. Kamat, James M. Burke, Kirk A. Keegan & Gary D. Steinberg

*Nature Medicine* **30**, 2216–2223 (2024) | Cite this article


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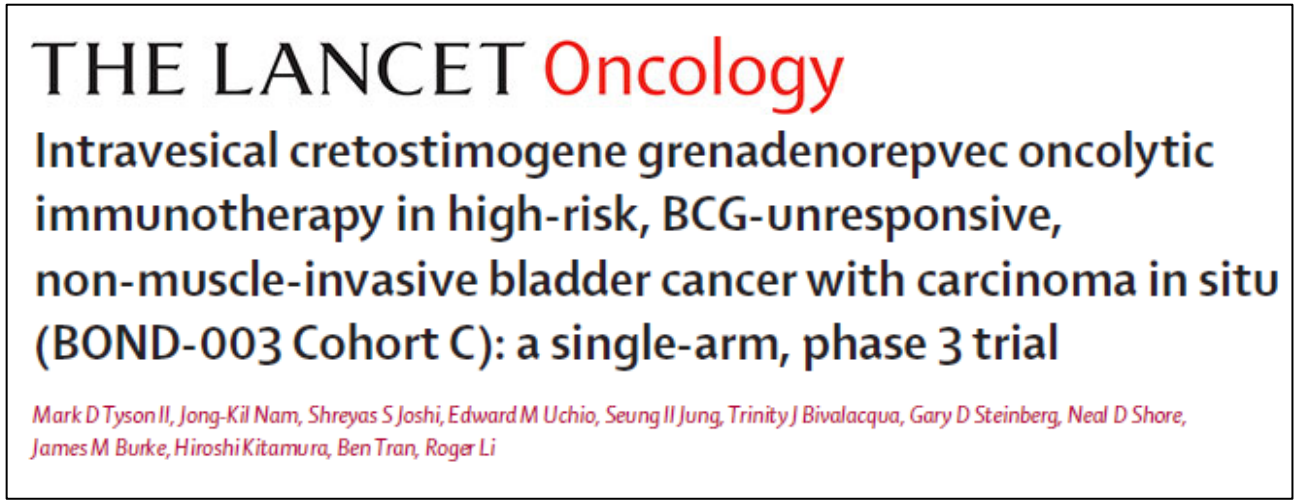
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Article | Published: 09 November 2024

**Oncolytic immunotherapy with nivolumab in muscle-invasive bladder cancer: a phase 1b trial**

Roger Li, Nancy Y. Villa, Xiaoqing Yu, Joseph O. Johnson, Gustavo Borjas, Jasreman Dhillon, Carlos M. Moran-Segura, Youngchul Kim, Natasha Francis, Denise Dorman, John J. Powers, Wade J. Sexton, Philippe E. Spiess, Michael A. Poch, Logan Zemp, Scott M. Gilbert, Jingsong Zhang, Julio M. Pow-Sang, Alexander R. A. Anderson, Tingyi Li, Xuefeng Wang, G. Daniel Grass, James M. Burke, Colin P. N. Dinney, ... Jose R. Conejo-Garcia + Show authors

*Nature Medicine* **31**, 176–188 (2025) | Cite this article


THE LANCET Oncology

**Intravesical cretostimogene grenadenorepvec oncolytic immunotherapy in high-risk, BCG-unresponsive, non-muscle-invasive bladder cancer with carcinoma in situ (BOND-003 Cohort C): a single-arm, phase 3 trial**

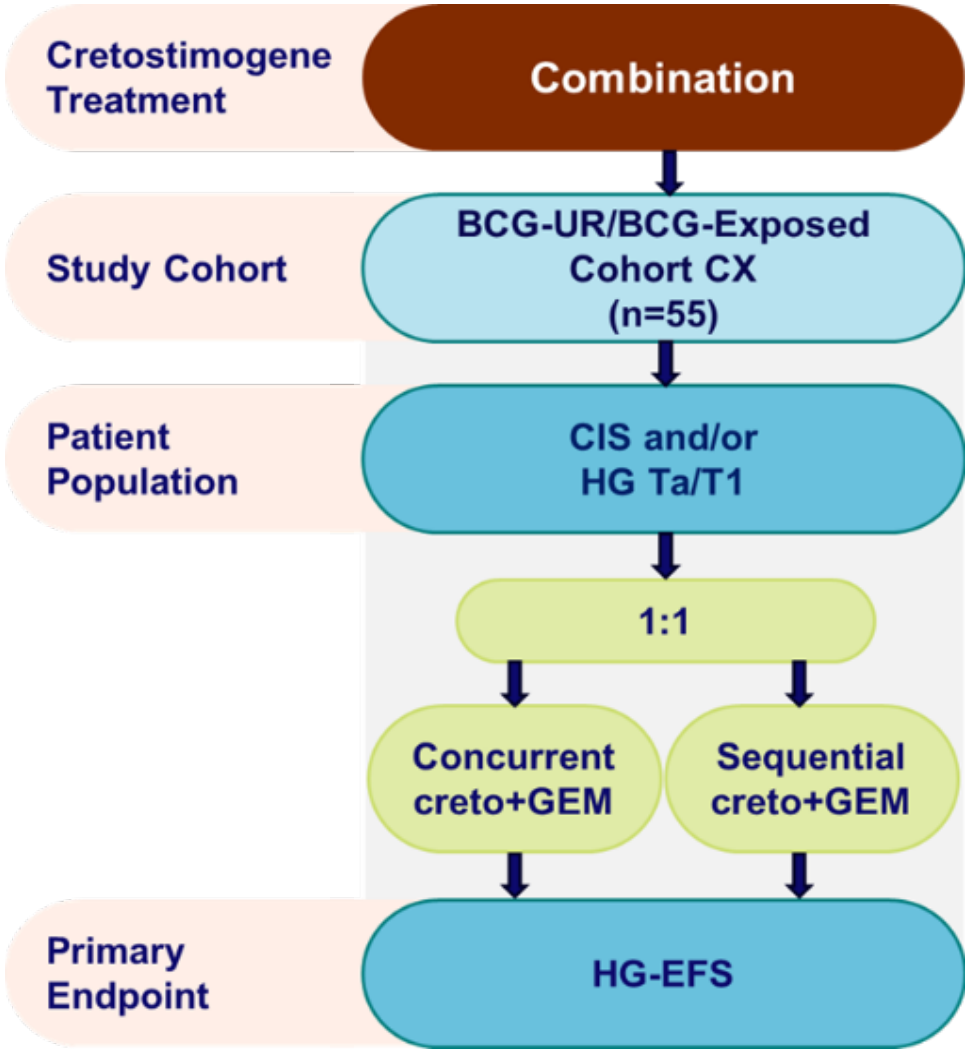
*Mark D Tyson II, Jong-Kil Nam, Shreyas S Joshi, Edward M Uchio, Seung Il Jung, Trinity J Bivalacqua, Gary D Steinberg, Neal D Shore, James M Burke, Hiroshi Kitamura, Ben Tran, Roger Li*

BCG: bacillus Calmette-Guérin; HR: high risk; IVE: intravesical; MIBC: muscle-invasive bladder cancer; NMIBC: non-muscle invasive bladder cancer; UR: unresponsive

1. Tyson M, et al. *Lancet Oncology* 2026. 2. Li R, et al. *Nat Med* 2024;30(8):2216-2223 3. Li, R, et al. *Nat Med* 2025; 31(1):176-188

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# Phase 2 Trial Design and Treatment Schedule




## BCG-Exposed

- Prior BCG *and*
  - Presented with CIS/HGTa recurrence at first evaluation (BCG-resistant) *or*
  - Recurred outside of the BCG-unresponsive window following adequate BCG, *or*
  - Recurred within 24 months after inadequate BCG

## BCG-Unresponsive

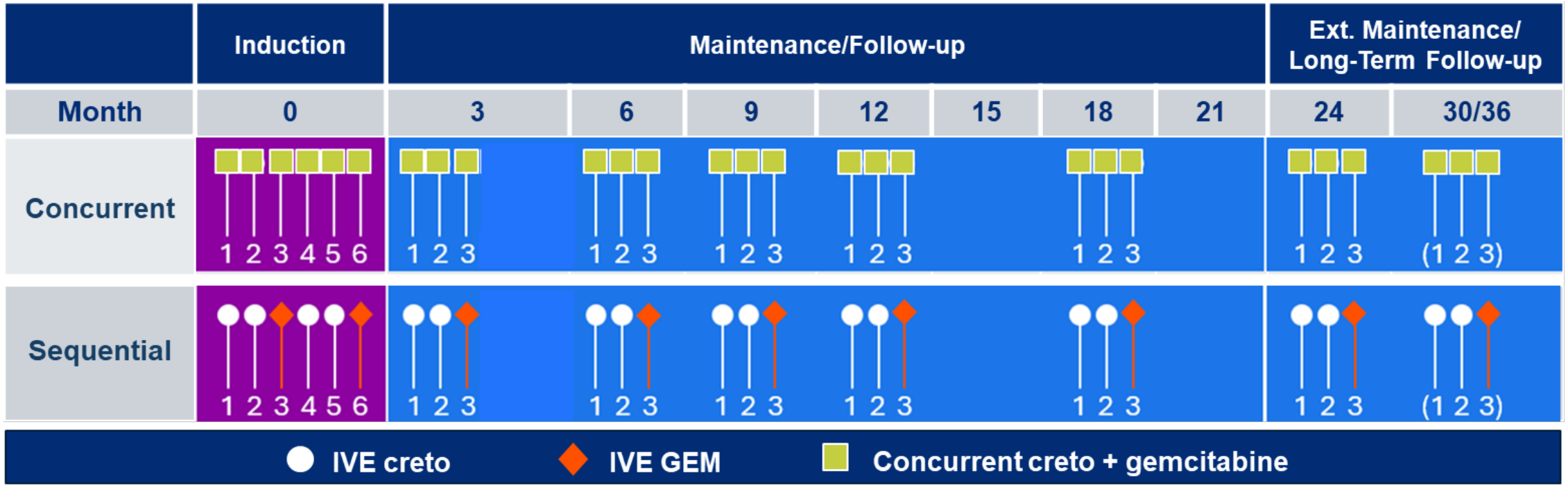
Participants who received adequate BCG (5+2) and present with

- HG T1 at first evaluation following induction course;
- HG Ta/T1 within 6 mo;
- CIS within 12 mo

BCG: bacillus Calmette-Guérin; CIS: carcinoma in situ; CR: complete response; CT: computed tomography; HG: high grade; HG-EFS: high-grade event-free survival;
Concurrent: Same-day administration of cretostimogene (first) followed by gemcitabine throughout induction and maintenance.
Sequential: Two weekly cretostimogene instillations followed by one gemcitabine instillation (Weeks 1, 2, 4, 5 vs Weeks 3, 6), continued in maintenance.
Efficacy assessments based on local pathology review.

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# Treatment & Assessment Schedule




- Re-induction allowed for patients with HG Ta and/or CIS at Month 3
- Assessments include cystoscopy & cytology every 3 months; CT/MRU every 6 months
- Clinic-based instillation

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# Patient Demographics & Baseline Characteristics

| Patients in Safety Dataset (N=55) | | |
|---|---|---|
| **Sex, Male n, %** | 43 | 78.2 |
| **Age in Years, Median, IQR** | 75 | (66-79) |
| **Age in Years, Categories, n %** | | |
| < 65 | 10 | 18.2 |
| ≥ 65 and < 75 | 17 | 30.9 |
| ≥75 | 28 | 50.9 |
| **ECOG PS, n, %** | | |
| 0 | 48 | 87.3 |
| 1 | 6 | 10.9 |
| 2 | 1 | 1.8 |
| **HR NMIBC T-Stage at Study Entry, n, %** | | |
| CIS +/- HG Ta/T1 | 28 | 50.9 |
| HG Ta/T1 | 27 | 49.1 |
| **BCG History, n, %** | | |
| Median BCG doses (IQR) | 7.0 | 6-13 |
| BCG-Exposed | 36 | 65.5 |
| BCG-Unresponsive | 19 | 34.5 |

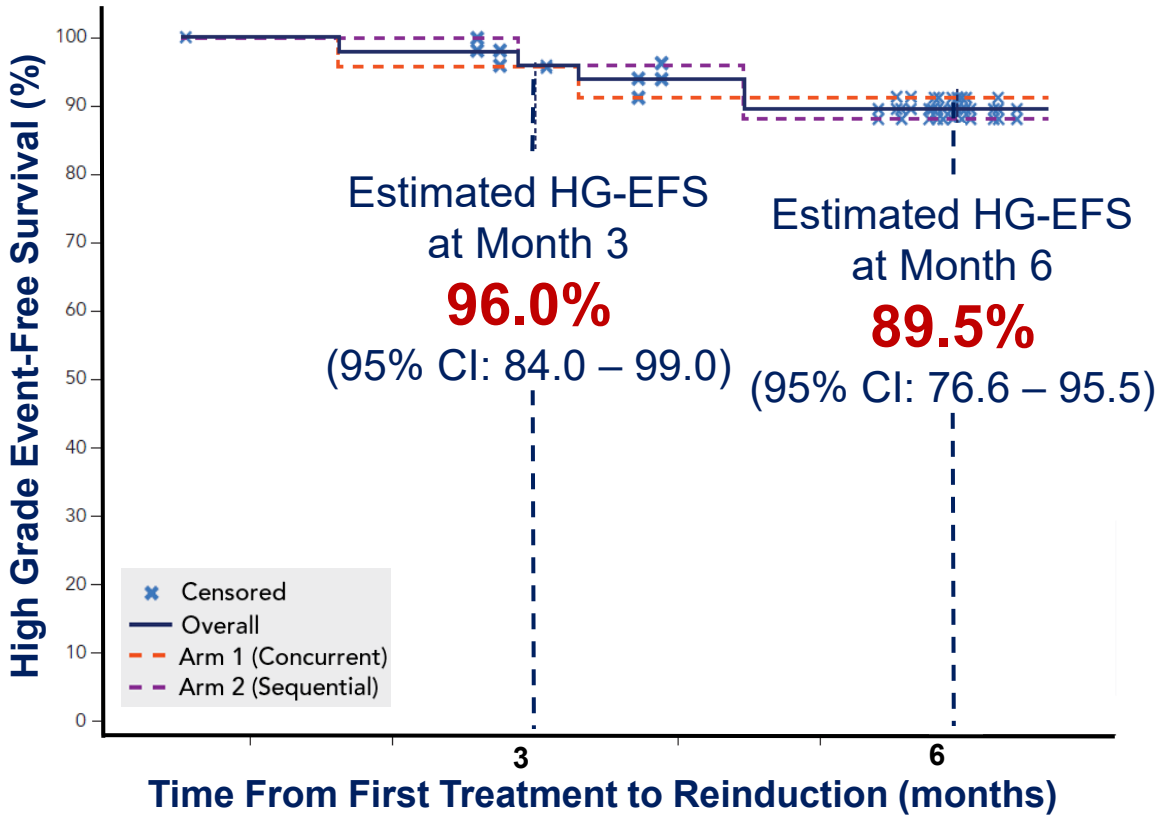
- All patients enrolled from the U.S.; multiple care sites
  - 80.0% community
  - 20.0% academic
- **Majority of patients are:**
  - Male (78.2%)
  - White (92.7%)
  - > 65 years (81.8%)
- Cohort generally well-balanced across concurrent and sequential treatment arms

BCG: bacillus Calmette-Guérin; CIS: carcinoma in situ; ECOG PS: Eastern Cooperative Oncology Group performance status; HG: high grade; HR: high risk; NMIBC: non-muscle invasive bladder cancer

# Efficacy in CORE-008 Cohort CX

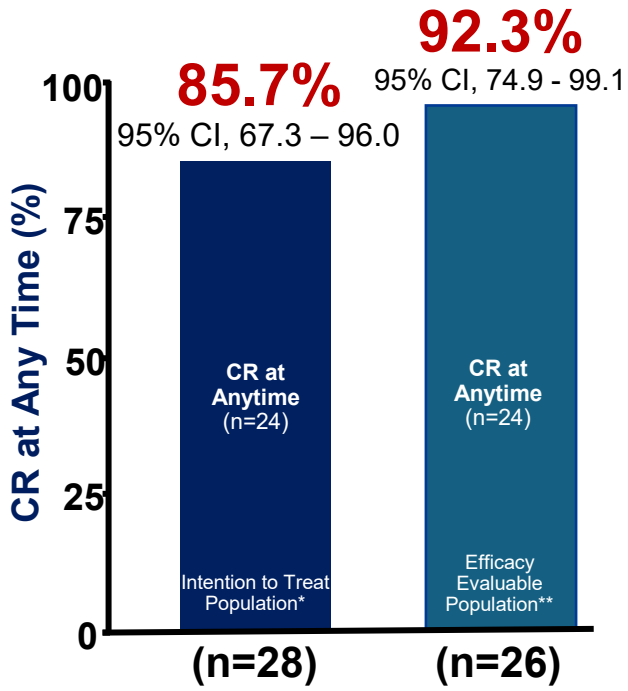
## Primary Endpoint: High-Grade Event-Free Survival

ITT, n=55




## Secondary Endpoint: CR at Any Time

CIS Containing Population




- High CR rates in both concurrent and sequential arms, with overlapping CIs
- CR outcomes directionally consistent with primary endpoint findings (HG-EFS)

| CR Rate | % (n/N) | 95% CI |
|---|---|---|
| Concurrent | **83.3%** *10 /12 patients* | (51.6, 97.9) |
| Sequential | **87.5%** *14 /16 patients* | (61.7, 98.5) |

Efficacy data cutoff as of 13MAR2026; efficacy assessments based on local pathology review.
BCG: bacillus Calmette-Guérin; CIS: carcinoma in situ; CR: complete response; HG: high grade; HG-EFS: high-grade event-free survival; ITT: intention to treat; HG-EFS defined as high-grade recurrence/persistence, progression to T1, progression to T2+ and death from any cause. CR defined as having negative cystoscopy, urine cytology, and biopsy (as indicated). CR analysis includes BCG-Exposed and BCG-Unresponsive patients. Two patients with CIS at baseline were found with HG T1 at Mo 6. *Intention to treat (ITT) population CX (Arm 1/Concurrent; Arm 2/Sequential). **Efficacy evaluable population includes patients who have received at least four doses of cretostimogene, meet the definition of BCG-Unresponsive/BCG-Exposed and have completed a protocol-defined efficacy assessment at Month 3. Includes all participants randomized.

# Favorable and Well-Tolerated Safety Profile

| Preferred Term (MedDRA v.26.1) | Overall (n=55) | |
|---|---|---|
| | Grade 1-2 n (%) | Grade ≥ 3 n (%) |
| **Patients with ≥ 1 TRAE** | 36 (65.5 %) | 0 (0) |
| **Treatment-Related AE reported in ≥ 10% patients** | | |
| Bladder Spasm | 26 (47.3) | 0 (0) |
| Dysuria | 19 (34.5) | 0 (0) |
| Pollakuria | 14 (25.5) | 0 (0) |
| Fatigue | 10 (18.2) | 0 (0) |
| Micturition Urgency | 8 (14.5) | 0 (0) |
| Hematuria | 6 (10.9) | 0 (0) |

- **0% Grade ≥ 3 TRAEs, SAEs or deaths**
- 85.5% (47/55) completed all protocol-defined treatments
  - Arm 1 (Concurrent)- 71.4% (20/28)
  - Arm 2 (Sequential)- 100% (27/27)
- **No patients discontinued on Arm 2 (sequential) due to TRAE**
- 4 patients withdrew from Arm 1 (concurrent) for persistent grade 1-2 localized TRAEs
- No difference in the proportion of patients with AEs between arms

Safety Data Cutoff Date 13MAR2026
AE: adverse event; MedDRA: Medical Dictionary for Regulatory Activities; SAE: serious adverse event; TRAE: treatment-related adverse event
Concurrent: Same-day administration of cretostimogene (first) followed by gemcitabine throughout induction and maintenance.
Sequential: Two weekly cretostimogene instillations followed by one gemcitabine instillation (Weeks 1, 2, 4, 5 vs Weeks 3, 6), continued in maintenance.

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# CORE-008 Cohort CX: Summary and Conclusions

- The combination of cretostimogene and gemcitabine demonstrates **robust clinical efficacy and safety** in BCG-exposed and BCG-unresponsive NMIBC
- **Comparable efficacy** observed in both concurrent and sequential arms
- Sequential administration of intravesical cretostimogene and gemcitabine was well-tolerated and supports the feasibility of intravesical-only treatment strategies
- **Continued follow-up is underway with SWOG ARCIS and CORE-008 Cohort E (xCEED) trials** to further characterize longer-term outcomes

BCG: bacillus Calmette-Guérin; NMIBC: non-muscle-invasive bladder cancer

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CORE-008
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BCAN
20 Years of Impact

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# THANK YOU

## Bladder Cancer Patients and Their Families
## Key Investigators, Study Coordinators, Nurses

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